# New advances in MDR treatment.

## Polymyxin and Nephroprotective agents.


By:

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# Introduction

NOIGEL LLC is a New York based company and established in 2010

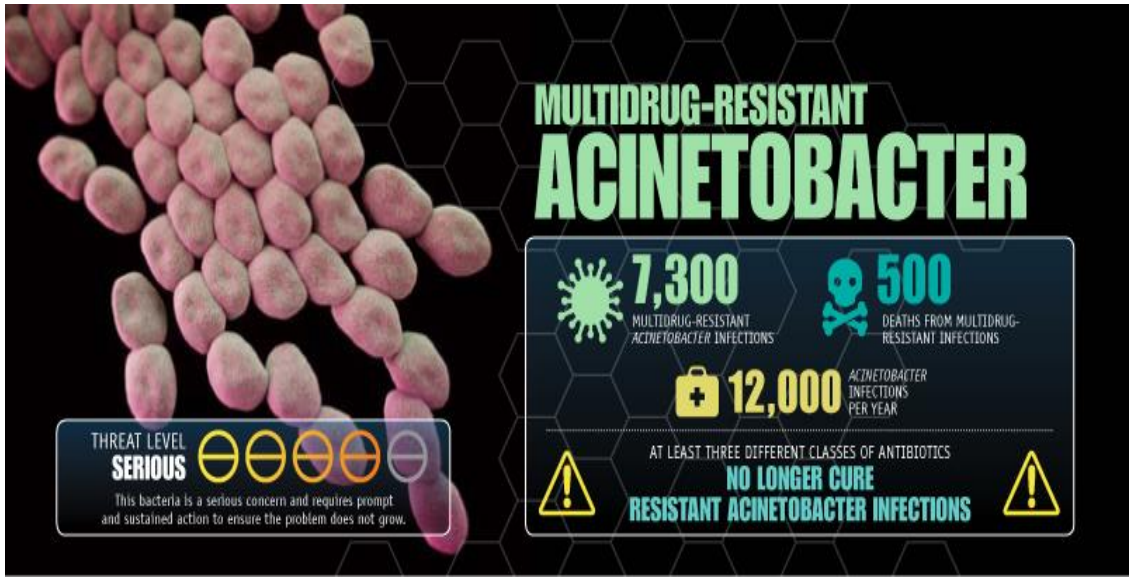
Our mission is to find new innovative ways to treat MDR infections.

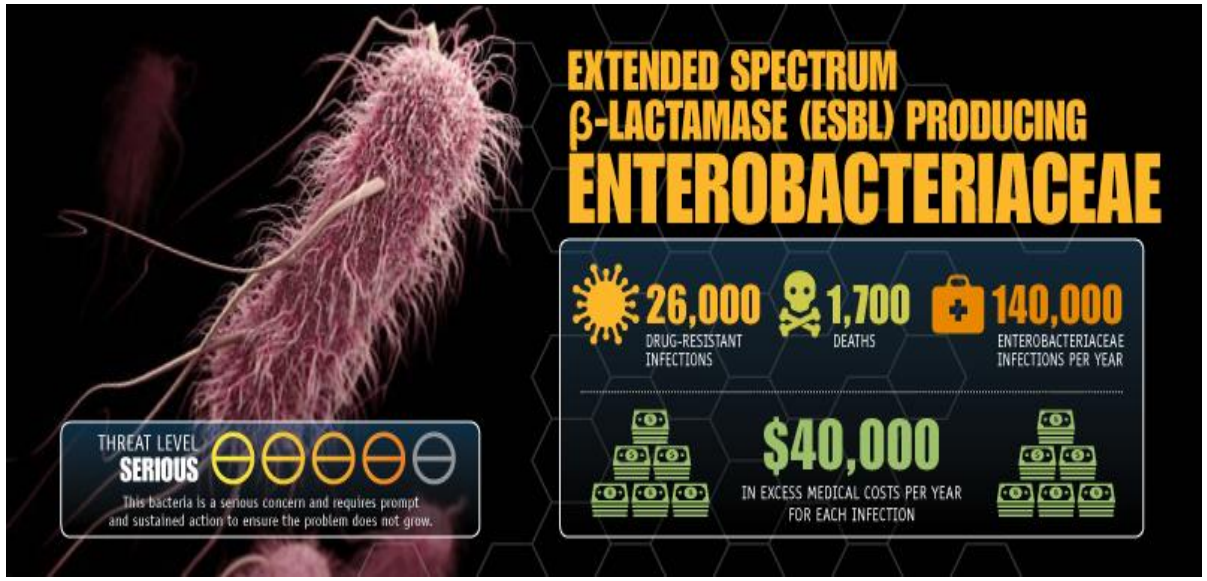
Amongst the company's expertise is utilizing synergistic combinations of **FDA approved generic drugs** and developing pharmaceutical compositions with new and unique applications.

NOIGEL scientists have published extensive research studies supporting development of their pharmaceutical compositions.

# CDC Statistics gram neg MDR threat

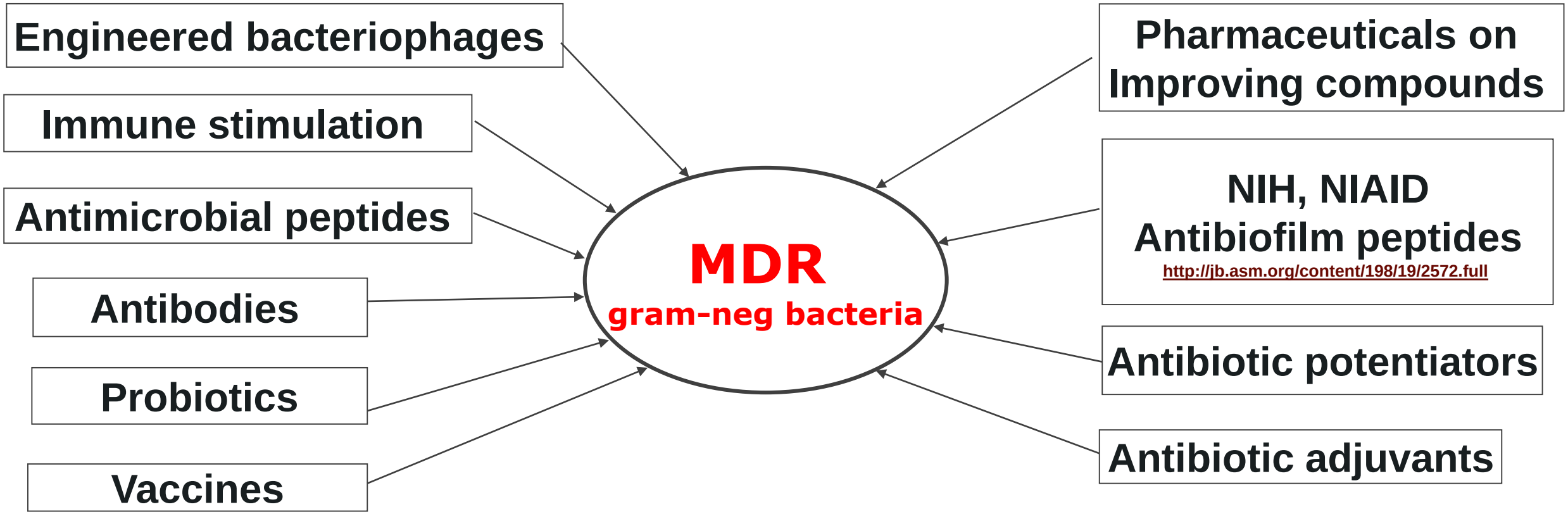





https://www.cdc.gov/drugresistance/biggest_threats.html

# Current research strategies within scientific community.



# The cost of antibiotic resistance to U.S. health care system

- A 2011 IDSA (Infectious Diseases Society of America) survey found more than 60 percent of surveyed infectious-disease specialists had seen a pan-resistant, untreatable bacterial infection within the prior year.
- HAIS **(Healthcare-Associated Infections)** cause **99,000 deaths** in the nation every year. Antibacterial-resistant pathogens cause most of these deaths.
- Sepsis and pneumonia caused nearly 50,000 U.S. deaths in 2006. These two HAIs cost the U.S. healthcare system more than **$8 million in 2006.**
- Antibiotic-resistant infections lengthen patients' hospital days by an average of 6.4 days to 12.7 days.
- Antibiotic-resistant infections cost the U.S. economy nearly **$20 billion in healthcare costs and $35 billion each year** lost productivity.

# Market Opportunity

**12**

Only 12 New antibiotics FDA approved in last 5 years *

**4-9%**

Annual Increas in global anti-MDR bacteria antibiotic market*

**$246 Mill. USD**

Amount to spend in Pharma and academia to fight MDR bacteria**

* https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm595264.htm

** http://www.globalopportunitynetwork.org/report-2016/new-business-model-for-antibiotics/

# Polymyxin and Nephrotoxicity

- Polymyxin B was first patented in 1952.
- Polymyxin nephrotoxicity has made it a less desirable treatment over the years.
- As per NIH report Polymyxin B has resurged in recent years as a **last resort** therapy for Gram-negative MDR and extremely drug resistant (XDR) infections.

**NOIGEL has developed pharmaceutical compositions that decrease Polymyxin's nephrotoxicity and increase efficiency to fight MDR bacteria.**

# Past strategies on Polymyxin Nephrotoxicity

- Polymyxin IV administration in different doses and different time ranges.[1]
- Analyzing drug delivery methods (e.g.s IV, IM or SQ).[2]
- Diverse methods of Polymyxin production and purification.[3]


1 http://www.scielo.br/pdf/ape/v26n1/en_10.pdf
2.http://www.scielo.br/pdf/ramb/v55n6/en_23.pdf
3.https://patents.google.com/patent/WO2010058427A2/en

# NOIGEL'S Research Project

## Research Base:

**NOIGEL LLC : Laboratory of Immunopharmacology**
**Laboratory of Biochemistry and Biotechnology**

## Testing Method

**NOIGEL performed in vivo testing of Polymyxin and NP200 based on Silico modeling method.**

## Intelectual Property IP

**NOIGEL has patented pharmaceutical compositions as a nephroprotectors, which can reduce and eliminate Polymyxin nephrotoxicity.**

# NOIGEL Nephroprotective agents - NP200

- Based on polymyxin affinity to megalin, NOIGEL has defined **Nephroprotective agents - NP200.**
- NOIGEL researched thousands of FDA approved drugs and substances.
- Research led to discovery of nephroprotective agents (NP200)
  - NP200 has higher affinity for megalin than polymyxin.
  - NP200 has low or no overall toxicity to kidneys.
  - NP200 can be administered along with a polymyxin without compromising it antibacterial efficacy.

# NOIGEL Proof of Concept

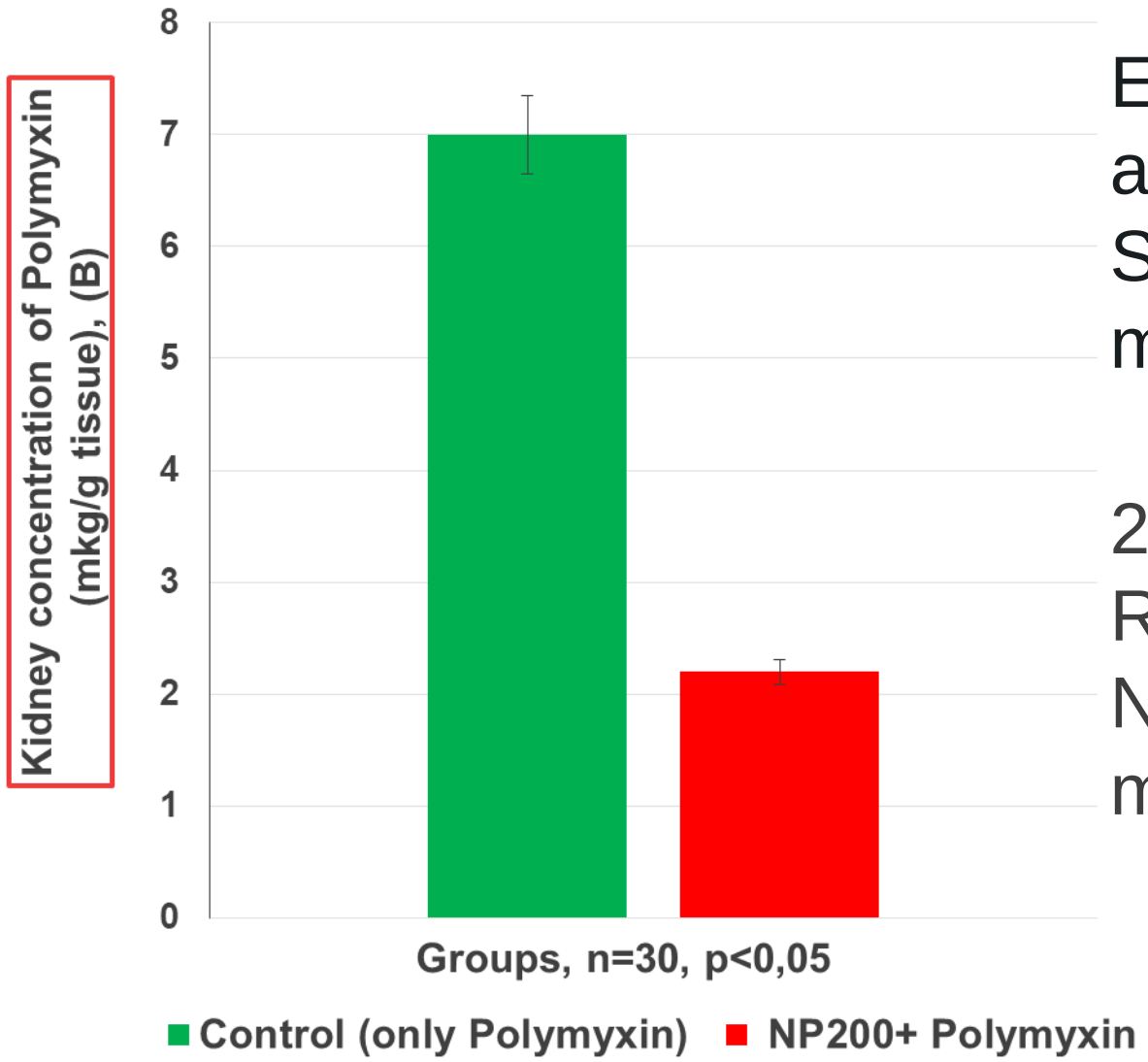
## Finding the most suitable Nephroprotective agents:

- NOIGEL identified 246 substances from 21,000 FDA approved generic drugs.
- NOIGEL selected two substances best suitable as Nephroprotective agents (NP200).

## Properties of NP200:

- NP200 is comprised of Quinones and Imidazole classes.
- NP200 has higher than Polymyxin affinity to kidney megalin receptor.
- NP200 has minimal spectrum of side effects to host body and doesn't affect Polymyxin antimicrobial activity.

# Polymyxin accumulation in the kidney

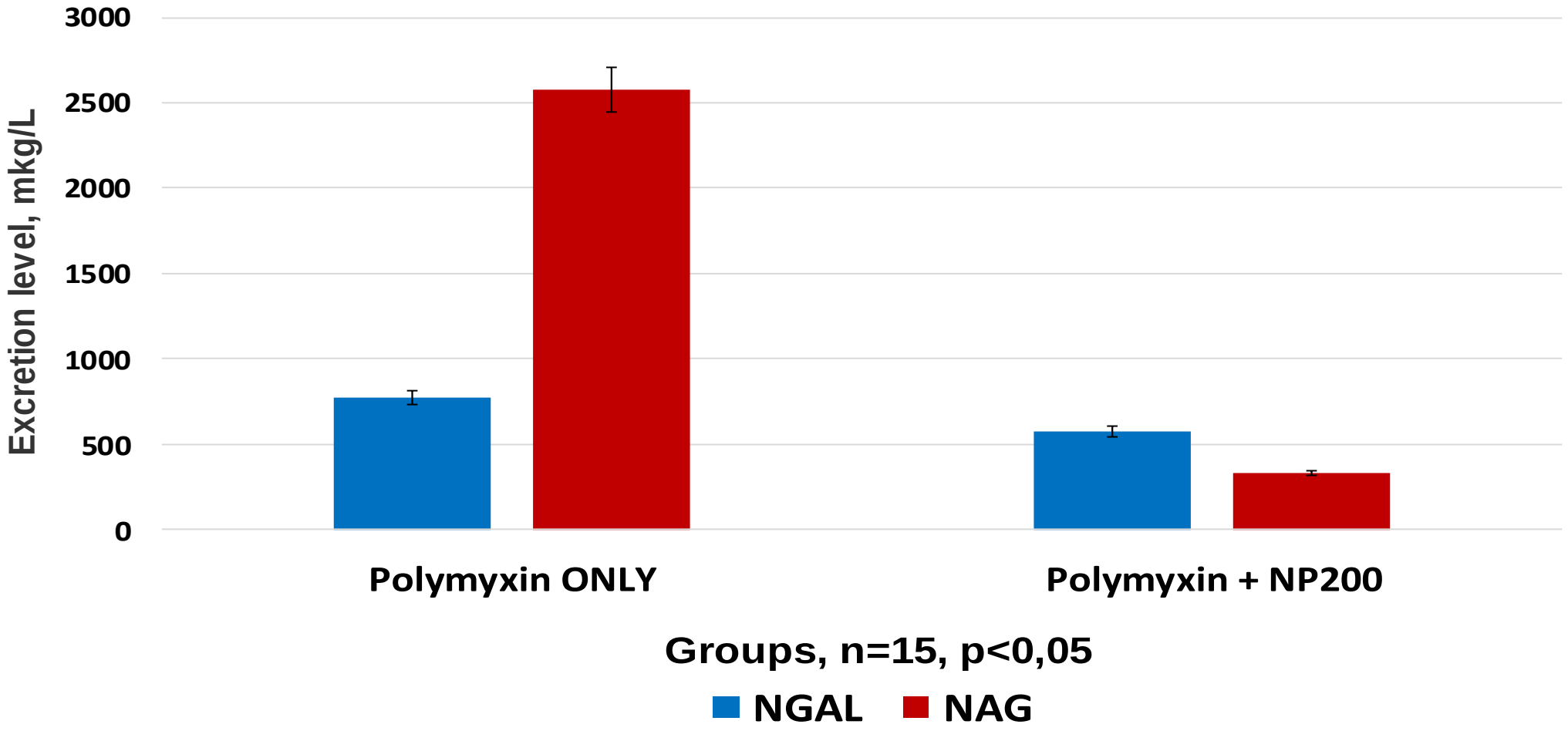



Experiment of 250 rats, ELISA-test and HPLC-systems were used. Studies were conducted during an 18 month period (in series).

2 groups(30 animals per group)
Results: 45 min after administration of NP200 (15 mg/kg) and colistin (0.5 mg/kg) intravenously (IV).

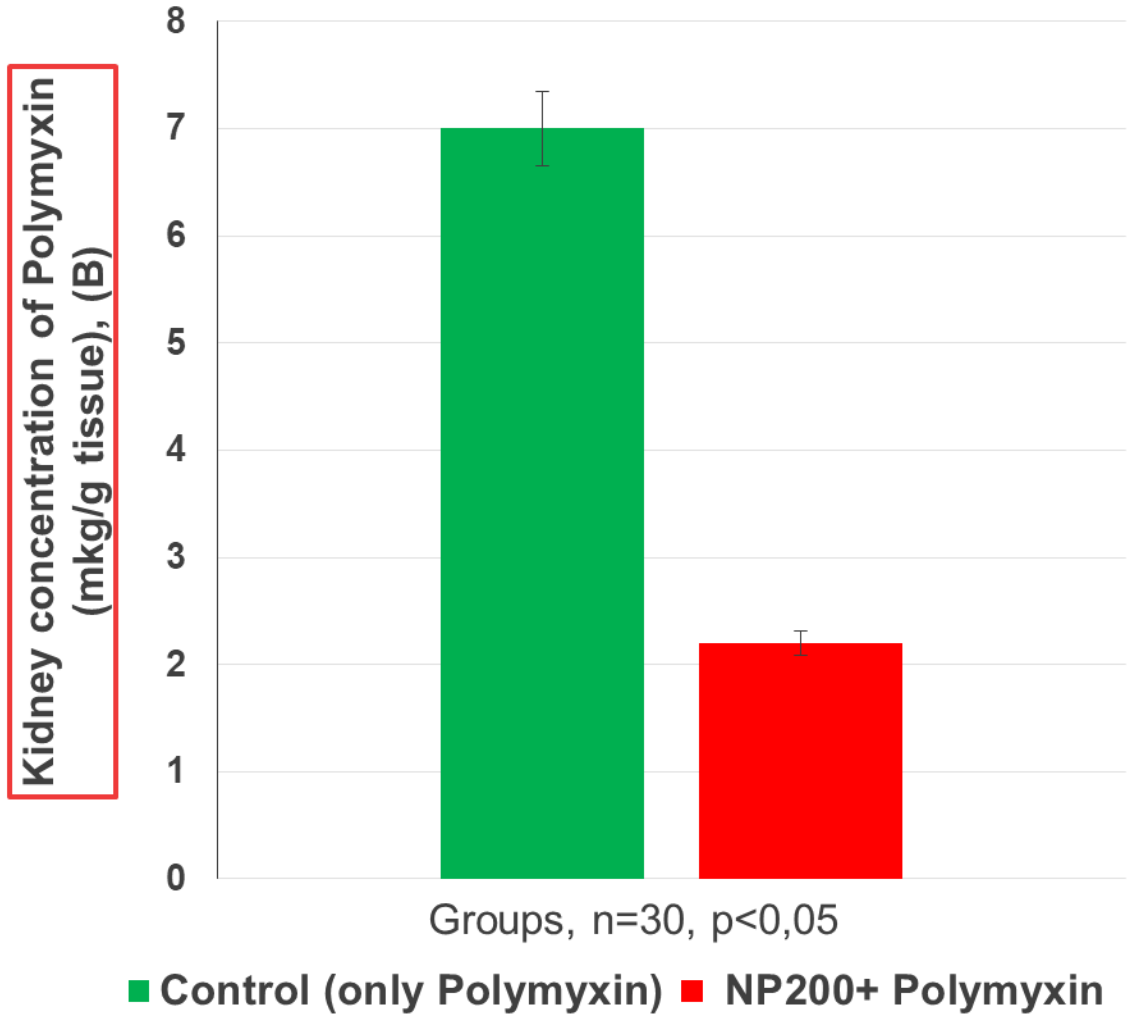
# Study: kidney injury Polymyxin and NP200

- Neutrophil gelatinase-associated lipocalin **(NGAL)** - biomarker of acute kidney injury. N-acetyl-beta-D- glucosaminidase **(NAG)** - biomarkers of kidney disease (the 30 days after the last administration of polymyxin the excretion level of both compounds < 120 mkg /L )

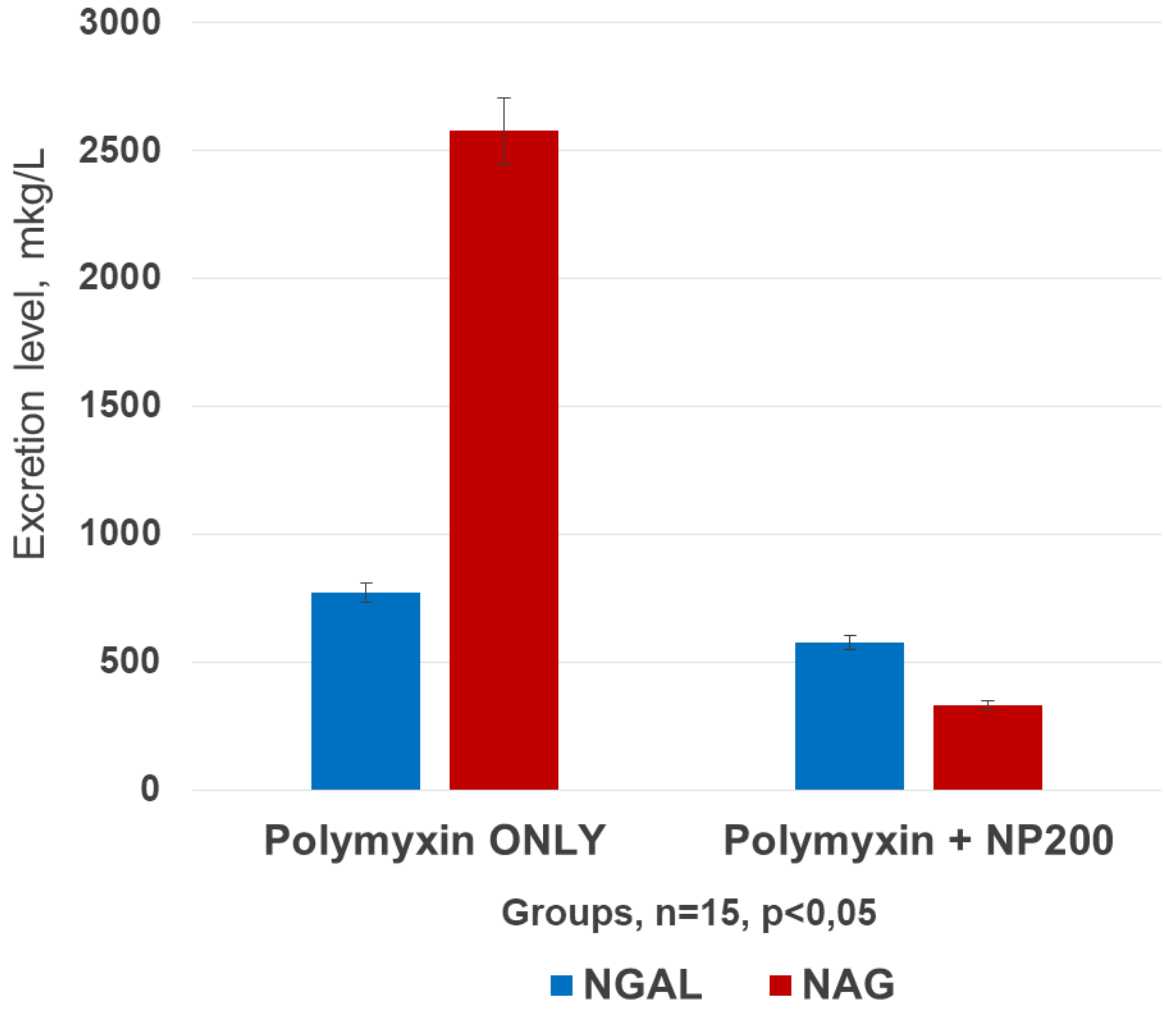


# Results: NP200 achieves goals

- Polymyxin kidney accumulation.




- Polymyxin nephrotoxicity biomarkers.



# Key Takeaways

- **No changes in the polymyxin chemical structure.**

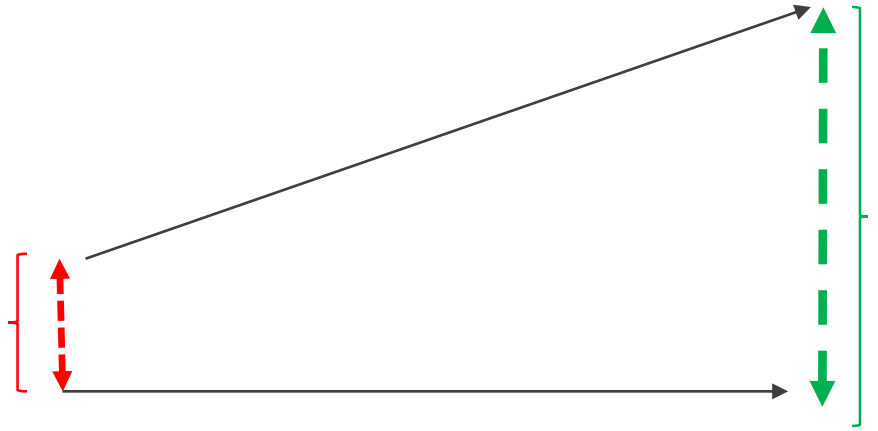
## Prospects for Polymyxin clinical use:

**Without NP200**

1week therapy **with risk of** nephrotoxicity.

**With NP200**

>1 week therapy **without or mild** nephrotoxicity.



The narrow range of action for infections that treatment can be stopped in 1 week

The broader range of action for infections that require longer treatment.

# Publications and IP for NP200

## IP:

1. **New combinatorial derivatives of antibiotics based on supramolecular structures PCT/RU2017/000424**
2. **Pharmaceutical composition for the treatment of infectious diseases based on polymyxin with nephroprotectors (Application filed 05/02/2018 with the PCT Patent Office)**

## Publications:


1. Lisnyak Y.V., Martynov AV (2012). Molecular modeling of antimicrobial compounds interactions with cell membrane elements: nystatin-ergosterol membrane pore. *AMI, (*3), 51-56.

2. Lisnyak Yu.V., Martynov A.V., Alhussein M., Prikolotin A.V. Drug-target interactions of polymyxins: A computational structure-toxicity study / 4th International Symposium "Methods and Applications of Computational Chemistry" - Lviv, 28 June - 2 July, 2011. Book of Abstracts.- Lviv-Kharkiv, 2011- P.105.

3. Lisnyak Yu.V. Gubskaya A. V., Martynov A.V. Molecular Modeling Study of Polyene-Sterol Membrane Channel //2nd International Symposium “Methods and Applications of Computational Chemistry”. – Kyiv, 2-4 July, 2007. – Book of Abstracts. – Kyiv-Kharkiv, 2007. – P.90.

# NEXT STEPS

## Nephroprotective agents NP200 with Polymyxin B can be leveraged in several ways:

- Pharmaceutical companies currently holding Polymyxin in their portfolio could use NOIGEL'S pharmaceutical composition to improve Polymyxin use efficiently and boost sales exponentially.
- Pharmaceutical companies currently holding generic Nephroprotective drugs NP200 in their portfolio could use them with additional new application, which will boost sales of NP200.
- Life Sciences private equity groups and venture capital firms could partner with NOIGEL.
- NOIGEL open for discussion of different types of collaboration as well.

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# Thank You For Your Time